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CONTRACTING ORGANIZATION: Thomas Jefferson University
Philadelphia, Pennsylvania 19107

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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

Decorin is a prototype member of a family of the so-called small leucine-rich proteoglycans. Recent evidence has shown that decorin down-regulates the growth of a variety of tumor cells including breast carcinoma cells. Specifically, we have previously shown that decorin blocks the ErbB2 activity and, therefore, we believe that this is the mechanism that is utilized by decorin-induced growth inhibition. In the past funded year, we have made an attempt to generate adeno-associated viral vector (AAV2) containing decorin. After several negative attempts, we were successful in generating an AAV1-decorin vector. In preliminary studies, we have shown that this vector is capable of transducing various tumor cell lines and generating decorin. We have requested and obtained a one-year, no cost extension to pursue the AAV1 transduction experiments both in vitro and in vivo, in an animal model of orthotopic breast cancer.

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INTRODUCTION

Decorin is a member of the small leucine-rich repeat proteoglycan gene family that is associated with collagen and also affects a variety of cellular functions including modulation of growth factors and the growth of tumor cells. We, and others, have previously shown that exogenous decorin or *de novo* expression of decorin can modulate the growth of a variety of tumor cells including breast carcinoma cells (1-5). The central hypothesis, therefore, of this concept award was to generate AAV vector containing decorin and to treat breast carcinoma cells *in vivo* using this method of gene transfer.

BODY OF WORK

In the past year and a half we have been actively working on generating an AAV vector containing the human decorin gene. After unsuccessful attempts to generate an AAV2, we focused our attention on AAV1 and we were able to generate overexpression of decorin in several tumor cell lines, including colon carcinoma and squamous cell carcinoma. However, in part because of the small amount of funding provided by the concept award and, in part, because of the short period of time given, we have not been able to make significant progress in this area of research. We are still attempting to generate a viable animal model of breast carcinoma. We have tested a number of cells and injected into the mammary gland of nude mice and we have not obtained any tumors. These studies have taken a significant amount of time and have precluded making any considerable progress.

KEY RESEARCH ACCOMPLISHMENTS

We were able to generate a vector that could be used in future studies to target breast cancer cells *in vivo*. This vector is based on the latest generation of AAV1 which can considerably induce expression of decorin in breast carcinoma cells and thus, retard the growth of breast carcinoma. Because this vector is stable, there could be effects even at distant sites because the decorin levels in the blood could also increase. Another advantage of this approach is that the vector could potentially be delivered systemically since it generates very little immune reaction.

REPORTABLE OUTCOMES

At this moment there are no reportable outcomes.

CONCLUSIONS

We have demonstrated that it is possible to generate an AAV1 vector containing decorin and that this vector can officially transduce tumor cell lines. These preliminary studies are encouraging and suggest that we will be able to pursue the study of breast tumor cells *in vivo* once we have established a viable animal model. Of importance is that we have recently published a paper in

Oncogene (6) in which we have shown that adeno virus-mediated gene transfer of decorin, a transient expression of decorin, is capable of suppressing tumorigenicity of colon and squamous cell carcinoma. This study is encouraging and suggests that AAV-decorin could have a significant affect in the treatment of breast carcinoma.

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